#14/B
5/17/01

23541.01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Peter Richard REEVES, et al.

Examiner: B. Sisson

Group Art Unit: 1655

Serial No.: 09/423,093

Filed: November 1, 1999

For: **NUCLEIC ACID MOLECULES SPECIFIC FOR BACTERIAL ANTIGENS AND USES THEREOF**

May 7, 2001

Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT

S I R:

In response to the Office Action dated December 18, 2000, please amend the above application as follows:

IN THE CLAIMS:

Cancel Claims 16 to 31 without prejudice and add the following claims:

43. (New) A method of testing a sample for the presence of *E.coli* expressing the bacterial polysaccharide O-antigen serotype 0111, the method comprising the steps:

(a) contacting the sample with at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 1 under conditions suitable to permit the at least one oligonucleotide molecule to specifically hybridise to at least one gene contained therein; and

(b) detecting any specifically hybridised oligonucleotide molecules.

44. (New) A method as claimed in Claim 43, wherein step (a) thereof involves contacting the sample with at least one pair of oligonucleotide molecules, at least one

oligonucleotide molecule of the pair capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 1 under conditions suitable to permit the at least one oligonucleotide molecule of the pair of molecules to specifically hybridise to at least one gene contained in SEQ ID NO: 1.

45. (New) A method as claimed in Claim 43, wherein said at least one oligonucleotide molecule is capable of specifically hybridising to nucleic acid sequences of the group consisting of:

wbdH (nucleotide position 739 to 1932 of SEQ ID NO: 1);

wzx (nucleotide position 8646 to 9911 of SEQ ID NO: 1);

wzy (nucleotide position 9901 to 10953 of SEQ ID NO: 1); and

wbdM (nucleotide position 11821 to 12945 of SEQ ID NO: 1).

46. (New) A method as claimed in Claim 43, wherein said at least one oligonucleotide molecule is chosen from the group consisting those oligonucleotides listed in tables 5 and 5A herein.

47. (New) A method of testing a sample for the presence of *E.coli* expressing the bacterial polysaccharide O-antigen serotype 0157, the method comprising the steps:

(a) contacting the sample with at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 2 under conditions suitable to permit the at least one oligonucleotide molecule to specifically hybridise to at least one gene contained therein; and

(b) detecting any specifically hybridised oligonucleotide molecules.

48. (New) A method as claimed in Claim 47, wherein step (a) thereof involves contacting the sample with at least one pair of oligonucleotide molecules, at least one oligonucleotide molecule of the pair capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 2 under conditions suitable to permit the at least one oligonucleotide molecule of the pair of molecules to specifically hybridise to at least one gene contained in SEQ ID NO: 2.

49. (New) A method as claimed in Claim 47, wherein said at least one oligonucleotide molecule is capable of specifically hybridising to the nucleic acid sequences of the group consisting of:

wbdN (nucleotide position 79 to 861 of SEQ ID NO: 2);

wbdO (nucleotide position 2011 to 2757 of SEQ ID NO: 2);

wbdP (nucleotide position 5365 to 6471 of SEQ ID NO: 2);

wbdR (nucleotide position 13156 to 13821 of SEQ ID NO: 2);

wzx (nucleotide position 2744 to 3109 of SEQ ID NO: 2); and

wzy (nucleotide position 858 to 2042 of SEQ ID NO: 2).

50. (New) A method as claimed in Claim 47, wherein said at least one oligonucleotide molecule is chosen from the group consisting of those oligonucleotides listed in tables 6 and 6a herein.

51. (New) A method of testing a sample for the presence of *S.enterica* expressing the bacterial polysaccharide O-antigen serotype C2, the method comprising the steps:

(a) contacting the sample with at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 3 under conditions suitable to permit the at least one oligonucleotide molecule to specifically hybridise to at least one gene contained therein; and

(b) detecting any specifically hybridised oligonucleotide molecules.

52. (New) A method as claimed in Claim 51, wherein step (a) thereof involves contacting the sample with at least one pair of oligonucleotide molecules, at least one oligonucleotide molecule of the pair capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 3 under conditions suitable to permit the at least one oligonucleotide molecule of the pair of molecules to specifically hybridise to at least one gene contained in SEQ ID NO: 3.

53. (New) A method as claimed in Claim 51, wherein said at least one oligonucleotide molecule is capable of specifically hybridising to the nucleic acid sequences of the group consisting of:

weaR (nucleotide position at 2352 to 3314 of SEQ ID NO: 3);

wbaL (nucleotide position 3361 to 3875 of SEQ ID NO: 3);

wbaQ (nucleotide position 3977 to 5020 of SEQ ID NO: 3);

wbaW (nucleotide position 6313 to 7323 of SEQ ID NO: 3);

wbaZ (nucleotide position 7310 to 8467 of SEQ ID NO: 3);

wzx (nucleotide position 1019 to 2359 of SEQ ID NO: 3); and

wzy (nucleotide position 5144 to 6313 of SEQ ID NO: 3).

54. (New) A method as claimed in Claim 51, wherein said at least one oligonucleotide molecule is chosen from the group consisting of those oligonucleotides listed in table 7 herein.

55. (New) A method of testing a sample for the presence of *S.enterica* expressing the bacterial polysaccharide O-antigen serotype B, the method comprising the steps:

(a) contacting the sample with at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 4 under conditions suitable to permit the at least one oligonucleotide molecule to specifically hybridise to at least one gene contained therein; and

(b) detecting any specifically hybridised oligonucleotide molecules.

56. (New) A method as claimed in Claim 55, wherein step (a) thereof involves contacting the sample with at least one pair of oligonucleotide molecules, at least one oligonucleotide molecule of the pair capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 4 under conditions suitable to permit the at least one oligonucleotide molecule of the pair of molecules to specifically hybridise to at least one gene contained in SEQ ID NO: 4.

57. (New) A method as claimed in Claim 55, wherein said at least one oligonucleotide molecule is capable of specifically hybridising to the nucleic acid sequences of the group consisting of:

wzx (nucleotide position 12762 to 14054 of SEQ ID NO: 4); and

wbaV (nucleotide position 14059 to 15060 of SEQ ID NO: 4).

58. (New) A method as claimed in Claim 55, wherein said at least one oligonucleotide molecule is chosen from the group consisting those oligonucleotides listed in table 8 therein.

59. (New) A method as claimed in any one of Claims 43, 47, 51, and 55, wherein the method further comprises contacting the sample with a further at least one oligonucleotide, or pair of oligonucleotides, capable of specifically hybridising to at least one sugar pathway gene under conditions suitable to permit the further at least one oligonucleotide to specifically hybridise to such gene of any bacteria expressing the bacterial polysaccharide antigen present in the sample and detecting any specifically hybridised nucleic acid molecules.

60. (New) A method as claimed in any one of Claims 43, 47, 51, and 55, wherein the specifically hybridised oligonucleotide molecules are detected by Southern blot analysis.

61. (New) A method as claimed in Claim 44, 48, 52 or 56, wherein the method is performed according to the polymerase chain reaction method.

62. (New) A method as claimed in any one of Claims 43, 47, 51, and 55, wherein said sample is a food derived sample.

63. (New) A method as claimed in any one of Claims 43, 47, 51, and 55, wherein said sample is a faecal derived sample.

64. (New) A method as claimed in any one of Claims 43, 47, 51, and 55 wherein said sample is derived from a patient.

65. (New) A kit for testing a sample for the presence of *E.coli* expressing the bacterial polysaccharide O-antigen serotype 0111, the kit comprising at least one

oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 1; the agents required for hybridisation of the oligonucleotide to the nucleic acid molecule SEQ ID NO: 1; and directions for the use thereof.

66. (New) A kit as claimed in Claim 65, wherein the at least one oligonucleotide molecule is capable of specifically hybridising to nucleic acid sequences of the group consisting of:

wbdH (nucleotide position 739 to 1932 of SEQ ID NO: 1);

wzx (nucleotide position 8646 to 9911 of SEQ ID NO: 1);

wzy (nucleotide position 9901 to 10953 of SEQ ID NO: 1); and

wbdM (nucleotide position 11821 to 12945 of SEQ ID NO: 1).

67. (New) A kit as claimed in Claim 65, wherein the at least one oligonucleotide molecule is chosen from the group consisting of those oligonucleotides listed in tables 5 and 5a herein.

68. (New) A kit for testing a sample for the presence of *E.coli* expressing the bacterial polysaccharide O-antigen serotype 0157, the kit comprising at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 2; the agents required for hybridisation of the oligonucleotide to the nucleic acid molecule SEQ ID NO: 2; and directions for the use thereof.

69. (New) A kit as claimed in Claim 68, wherein the at least one oligonucleotide molecule is capable of specifically hybridising to nucleic acid sequences of the group consisting of:

wbdN (nucleotide position 79 to 861 of SEQ ID NO: 2);

wbdO (nucleotide position 2011 to 2757 of SEQ ID NO: 2);

wbdP (nucleotide position 5365 to 6471 of SEQ ID NO: 2);

wbdR (nucleotide position 13156 to 13821 of SEQ ID NO: 2);

wzx (nucleotide position 2744 to 3109 of SEQ ID NO: 2); and

wzy (nucleotide position 858 to 2042 of SEQ ID NO: 2).

70. (New) A kit as claimed in Claim 68, wherein the at least one oligonucleotide molecule is chosen from the group consisting of those oligonucleotides listed in tables 6 and 6a herein.

71. (New) A kit for testing a sample for the presence of *S.enterica* expressing the bacterial polysaccharide O-antigen serotype C2, the kit comprising at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 3; the agents required for hybridisation of the oligonucleotide to the nucleic acid molecule SEQ ID NO: 3; and directions for the use thereof.

72. (New) A kit as claimed in Claim 71, wherein the at least one oligonucleotide molecule is capable of specifically hybridising to nucleic acid sequences of the group consisting:

weaR (nucleotide position at 2352 to 3314 of SEQ ID NO: 3);

wbaL (nucleotide position 3361 to 3875 of SEQ ID NO: 3);

wbaQ (nucleotide position 3977 to 5020 of SEQ ID NO: 3);

wbaW (nucleotide position 6313 to 7323 of SEQ ID NO: 3);

wbaZ (nucleotide position 7310 to 8467 of SEQ ID NO: 3);

wzx (nucleotide position 1019 to 2359 of SEQ ID NO: 3); and

wzy (nucleotide position 5144 to 6313 of SEQ ID NO: 3).

73. (New) A kit as claimed in Claim 71, wherein the at least one oligonucleotide molecule is chosen from the group consisting of those oligonucleotides listed in tables 7 and 7a herein.

74. (New) A kit for testing a sample for the presence of *S.enterica* expressing the bacterial polysaccharide O-antigen serotype B, the kit comprising at least one oligonucleotide molecule capable of specifically hybridising to the nucleic acid sequence SEQ ID NO: 4; the agents required for hybridisation of the oligonucleotide to the nucleic acid molecule SEQ ID NO: 4; and directions for the use thereof.

75. (new) A kit as claimed in Claim 74, wherein the at least one oligonucleotide molecule is capable of specifically hybridising to nucleic acid sequences of the group consisting:

wzx (nucleotide position 12762 to 14054 of SEQ ID NO: 4); and

wbaV (nucleotide position 14059 to 15060 of SEQ ID NO: 4).

76. (New) A kit as claimed in Claim 74, wherein the at least one oligonucleotide molecule is chosen from the group consisting of those oligonucleotides listed in tables 8 and 8a herein.

77. (New) An isolated nucleic acid molecule selected from the group consisting of the following sequences:

SEQ ID NO: 1;

nucleotide position 739 to 1932 of SEQ ID NO: 1;

nucleotide position 9982 to 10953 of SEQ ID NO: 1;

nucleotide position 11821 to 12945 of SEQ ID NO: 1;

SEQ ID NO: 2;

nucleotide position 79 to 861 of SEQ ID NO: 2;

nucleotide position 858 to 2042 of SEQ ID NO: 2;

nucleotide position 2011 to 2757 of SEQ ID NO: 2;

nucleotide position 2744 to 3109 of SEQ ID NO: 2;

nucleotide position 5365 to 6471 of SEQ ID NO: 2; and

nucleotide position 13156 to 13821 of SEQ ID NO: 2.

78. (New) A nucleic acid molecule derived from any one of the sequences defined in Claim 77 which nucleic acid molecules are capable of hybridising to the complementary sequence of the sequences defined therein.

79. (New) An isolated nucleic acid molecule which is any one of the oligonucleotides in table 5 or 5a herein.

80. (New) An isolated nucleic acid molecule which is any one of the oligonucleotides in table 6 or 6a herein.

81. (New) An isolated nucleic acid molecule selected from the group consisting of the following sequences:

SEQ ID NO: 3;

nucleotide position 1019 to 2359 of SEQ ID NO: 3;

nucleotide position 2352 to 3314 of SEQ ID NO: 3;

nucleotide position 3361 to 3875 of SEQ ID NO: 3;

nucleotide position 3977 to 5020 of SEQ ID NO: 3;

nucleotide position 5114 to 6313 of SEQ ID NO: 3;

nucleotide position 6313 to 7323 of SEQ ID NO: 3;

nucleotide position 7310 to 8467 of SEQ ID NO: 3;

SEQ ID NO: 4;

nucleotide position 12762 to 14054 of SEQ ID NO: 4; and

nucleotide position 14059 to 15060 of SEQ ID NO: 4.

82. (New) A nucleic acid molecule derived from any one of the sequences defined in Claim 81 which nucleic acid molecules are capable of hybridising to the complementary sequence of the sequences defined therein.

83. (New) An isolated nucleic acid molecule which is any one of the oligonucleotides in table 7 herein.

84. (New) An isolated nucleic acid molecule which is any one of the oligonucleotides in table 8 herein.

REMARKS

In the amendments above, Claims 1 to 42 have been cancelled in favor of new Claims 43 to 84, to more particularly point out and distinctly claims Applicant's invention. New Claims 43 to 64 correspond to cancelled Claims 16 to 31. Also, new Claims 65 to 76 correspond to cancelled Claims 32 to 42, and new Claims 77 to 84 correspond to cancelled Claims 1 to 11.

According to the Office Action, the Examiner has made an earlier-expressed restriction requirement FINAL. Applicants submit that there is a significant relationship between the sequences set forth in Claims 43 to 64 (i.e., Group III), and the subject matter set forth in remaining Claims 65 to 85, is such that the searching would necessarily be somewhat coextensive. Again, reconsideration and withdrawal of the restriction requirement is hereby requested.

While the Examiner initially requested a substitute specification, that request was modified to a request that Applicants correct any unclear idiomatic usage. The Examiner's reconsideration of his initial request is appreciated; however, Applicants are unable to discern any idiomatic usage that should be clarified. If the Examiner would point out specific instances of unacceptable idiomatic usage, Applicants would promptly make appropriate correction thereto.

Claims 16-31 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Also, Claims 16-31 have been rejected under § 112, first paragraph, as containing subject matte which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Further, Claims 16-31 have been rejected under 353 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which Applicants regard as the invention, and as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

The Examiner's attention is directed to the amendments above, wherein the originally-filed claims have been substantially revised. More specifically, the method claims are directed to methods for the identification of certain species of bacteria employing oligonucleotide molecules which are either characterised by their ability to specifically hybridize to specific nucleic acid sequences (for example SEQ ID NO:1), or by comprising a specific nucleic acid sequence (such as those identified in tables 5 and 5A), such sequences being clearly identified within the specification. Accordingly, Applicants submit that the breadth of the claims is commensurate with the description provided and clearly indicates that they were in possession of the invention defined therein at the time the application was filed.

Further, Applicants submit that the description provided within the specification is sufficient to teach a person skilled in the art how to make and use the full scope of the invention as claimed (in the amended claims herewith), without any undue experimentation. First, the starting materials needed to perform the invention are fully described; either the template nucleic acid (for example SEQ ID NO:1) or the specific oligonucleotides (for example those provided in Tables 5 and 5A). Where the specific physical characteristics (length and sequence) of an oligonucleotide of use in the invention is not elucidated, a person of ordinary skill in the art would readily be able to identify such characteristics based on the description provided within the specification; the specification teaches a length of at least 10-12 nucleotides, and the oligonucleotides must be capable of specifically hybridizing to the target nucleic acid sequences, which are specifically identified.

Second, it would be clear to a skilled person, from a reading of the specification, under what conditions a method according to the invention is to be practiced. In the case of the use of oligonucleotides specifically identified within the specification, suitable hybridisation conditions have been exemplified which allow for the specific detection of bacterial species, alone or in combination with a second oligonucleotide. With respect to the invention relating to oligonucleotides whose physical characteristics have not been

elucidated, Applicants submit that suitable hybridization conditions may readily be identified based on the sequence and length of a chosen oligo, knowledge of the target sequence to which the oligo is to hybridize, and common knowledge of the thermal stability of specific base pairs. The use of simple, readily available, and routinely used, computer programs, may also facilitate identification of suitable oligonucleotides and hybridisation conditions.

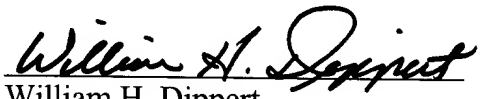
As should be appreciated, the nucleic acid molecule claims have been limited to those molecules specifically identified within the text of the specification. Accordingly, the invention defined in such claims is sufficiently supported by the description provided within the specification.

Applicants respectfully submit that the claims herein fully comply with the first and second paragraphs of § 112. Thus, the rejections based upon those paragraphs should be withdrawn.

In the event that the claims herein are in allowable condition but for matters that could be the subject of an Examiner's Amendment or a supplemental submission by Applicants, Applicants would appreciate the Examiner's contacting applicants' undersigned attorney.

Reconsideration and allowance of the claims herein are respectfully requested.

Respectfully submitted,



William H. Dippert
Reg. No. 26,723

Cowan, Liebowitz & Latman, P.C.
1133 Avenue of the Americas
New York, NY 10036-6799
Tel: (212) 790-9200